Clinical efficacy of trivalent oral poliomyelitis vaccine: a case–control study*

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A case–control study was carried out between May 1988 and May 1989 to assess the effectiveness of three doses of trivalent oral poliomyelitis vaccine ($TOPV_3$) in children aged 6–35 months in Madras city. All the cases were patients with acute paralytic poliomyelitis who were residing in Madras city and were hospitalized in the Institute of Child Health; they represented 95% of such cases in the city. The diagnosis was based on clinical grounds and confirmed by stool culture which was positive in 60%. Age- and sex-matched controls, all residing in the city of Madras, were recruited concurrently from the Institute's outpatient department. There were 78 cases and 315 controls. Vaccine efficacy observed for $TOPV_3$ was 81% (95% CI, 58–91%) for the 6–35-month age group and 86% (95% CI, 68–94%) for the 6–23-month age group. Vaccine efficacy, after controlling for age using the Mantel-Haenszel method, was 83% (95% CI, 67–91%). An unimmunized child was at 5 times greater risk of developing acute paralytic poliomyelitis than a fully immunized child.

Reports, mostly in the Indian literature, indicate an increasing proportion of acute paralytic poliomyelitis (APM) among children who had been immunized with three doses of trivalent oral poliomyelitis vaccine ($TOPV_3$, with 70–85% coverage), ranging from 10% to 26% among hospital studies (*1–4*). The immunogenicity of the vaccine has been assessed by the antibody response (seroconversion) to vaccination in ideal situations (*5*). Although seroconversion is a good criterion, it cannot be equated with the clinical protective efficacy that is actually observed in the community setting. It is therefore important to evaluate the efficacy of $TOPV_3$ on the basis of the immunization schedule in use. The present case–control study assesses the clinical efficacy of $TOPV_3$.

Patients and methods

This study was carried out at the Institute of Child Health, Madras, between May 1988 and May 1989. This hospital, one of the national sentinel centres for poliomyelitis, receives 95% of the APM cases in Madras city for hospitalization. All the cases (patients) and controls were recruited in the age group of 6–35 months and had to be residents of Madras city for homogeneity. The case definition for APM was based on clinical criteria (*6*)—namely, an acute, asymmetric flaccid paralysis of lower motor neurone type without any sensory disturbance, following a short episode of fever. Flaccid paralysis due to other causes like polyneuritis and hypokalaemia were excluded. Four controls (age- and sex-matched) for each case were recruited concurrently from the outpatient department. Age of the controls were matched exactly to cases <12 months old, or within ±1 month for cases aged 12–23 months and ±2 months for those >23 months old. Controls were from patients with minor illnesses (upper respiratory infection, fever, diarrhoea, etc.). Cases and controls were considered as immunized if they had received 3 primary doses of TOPV before 6 months of age (given at one month intervals, starting at 6–8 weeks of age). Immunization status was ascertained by questioning after recruitment and confirmed if records were available. The children were recruited by the same person (Research Officer) and all the case-patients were examined by the principal investigator (N.D.) at the time of recruitment.

Statistical methods. These included unmatched case–control analysis, and calculation of odds ratios (*OR*) for 1, 2 or 3 doses of $TOPV_3$, as well as vaccine efficacy (*VE*) using the formula, $VE = 1\text{–}OR \times 100$. In addition, Mantel-Haenszel (MH) odds ratios were calculated controlling for age and for immunization status individually.

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Results

The age distribution of cases (n = 78) and controls (n = 315) is given in Table 1. Since the age-matching of controls with cases was not exact for children >12 months old, the ratio of 4:1 is not uniform for these age groups. Confirmatory immunization cards were available for only 5% of cases as well as controls; 18 out of the 78 cases (23%) and 23 out of the 315 controls (7%) were unimmunized, while 46% (36/78) of the cases and 76% (240/315) of the controls had received 3 doses of TOPV. The odds ratios and vaccine efficacies with 95% confidence intervals (CI) for 1, 2 and 3 doses of TOPV in 6–35-month-olds and in 6–23-month-olds are presented in Table 2. The OR and VE (with 95% CI) after controlling for age, using the Mantel-Haenszel method for 3 doses of TOPV, were 0.169 (0.087, 0.331) and 83% (67%, 91%) respectively. As the number of doses increased from 1 to 3, there is a trend for increase in VE for both the 6–35 and 6–23 months age groups (P <0.001). An unimmunized child was at 5 times greater risk of developing paralysis than fully immunized children; those who received 1 and 2 doses were at 4.2 and 2.8 times greater risk, respectively.

Table 1: **Age distribution of cases (with poliomyelitis) and controls**

Age (months)	No. of cases	No. of controls
6–11	21 (26.9)[a]	95 (30.2)
12–33	40 (51.3)	175 (55.5)
24–35	17 (21.8)	45 (14.3)
Total	78	315

[a] Figures in parentheses are percentages.

Table 2: **Odds ratios and vaccine efficacies with their confidence intervals (95% CI) for 1, 2 and 3 doses of TOPV in 6–35-month-olds and 6–23-month-olds**

TOPV doses	No. of cases	No. of controls	Odds ratio	Vaccine efficacy (%)
6–35-month-olds:[a]				
0	18	23	1.0	
3	36	240	0.19	80.8
			(0.09, 0.41)[b]	(59, 91)
2	16	39	0.52	47.6
			(0.21, 1.33)	(–33, 79)
1	8	13	0.79	21.4
			(0.23, 2.62)	(–16, 77)
6–23-month-olds:[c]				
0	18	19	1.0	
3	27	204	0.14	86
			(0.06, 0.32)	(68, 94)
2	10	35	0.30	70
			(0.10, 0.86)	(14, 90)
1	6	12	0.53	47
			(0.14, 1.96)	(–96, 86)

[a] χ^2 trend: 29.2; P <0.001.
[b] Figures in parentheses are the 95% confidence intervals.
[c] χ^2 trend: 32.31 ; P <0.001.

Discussion

This study measured the protective efficacy of $TOPV_3$ under field situations in the city of Madras. The efficacies of $TOPV_3$ in the age groups 6–35 months and 6–23 months were not very different as indicated by the overlapping of confidence intervals in both groups. This small difference is probably due to the recalling ability being more positive for younger children. The OPV coverage for Madras city through the universal immunization programme for under-one-year olds during the study period was 87%. The vaccine failure in the age group, 12–23 months, was 50% (22/44) while vaccine efficacy was estimated to be 89%, which agrees with the value (90%) given by the series of curves constructed earlier for assessing the vaccine efficacy (*7*). The vaccine efficacy reported in North Arcot District, Tamil Nadu, South India was 61% and 72%, respectively, for the under-5-years and 12–23-months age groups (*8*). Similarly, in Gambia the VE for ≥3 doses was 72% in children aged 1 to 7 years (*9*). The VEs we obtained were higher, 81% (95% CI, 58–91%) and 86% (95% CI, 68–94%) for the 6–35-months and 6–23-months age groups, respectively. This is probably due to improved transportation and storage of vaccines in the city compared with the rural areas and also the difference in age periods (ability to recall). Our observation is similar to the estimated field efficacy of 90% in Bombay city based on the data from coverage surveys of children aged 12–23 months and immunization status of cases (*10*). The VE of a case–control study in a similar age group, 5–24 months, in Oman was 91% (*11*). The VE by case–control study for two countries in Taiwan for three or more TOPV doses in children aged 12 to 35 months was estimated to be 96% (*12*). A recent report of a case–control study in Delhi, using neighbourhood controls, has estimated VE to be 92% (*13*). Seroconversion rates in ideal situations for the three types of poliomyelitis vaccine were 75–80% (*5*).

An unimmunized child was at 5 times greater risk than an immunized child of developing poliomyelitis. However, the reported risk was 80 times when independent of sanitation facilities at home (*12*). This study has the limitations of case–control studies in general, but the following steps were taken. (1) Recall bias was minimized by having the

same paediatrician to select within the age group 6–35 months and ascertain the variables, giving the same emphasis to both cases and controls; the immunization history was taken only after recruitment of the subject. (2) Misclassification of cases and controls was avoided by adopting a uniform case definition and recruiting only after a thorough clinical examination; diagnosis of cases was confirmed by stool culture which was positive in 60%. (3) To avoid mismatching with respect to area of residence, cases and controls from only Madras city were accepted; it could have been better if controls were selected from the immediate neighbourhood of the cases. Since the cases and controls coming to our Institution from Madras city are from the same/similar socioeconomic status and environment, the bias due to sociodemographic differences is unlikely. It is concluded that the efficacy of 3 doses of TOPV in Madras city for children aged 6–23 months was 86% during the period of study.

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Résumé

Efficacité clinique du vaccin antipoliomyélitique buccal trivalent: étude cas-témoins

Une étude cas-témoins a été réalisée entre mai 1988 et mai 1989 pour évaluer l'efficacité de trois doses de vaccin antipoliomyélitique buccal trivalent ($TOPV_3$) chez des enfants âgés de 6 à 35 mois, dans la ville de Madras. Tous les cas étaient des malades atteints de poliomyélite paralytique aiguë, qui habitaient à Madras et étaient hospitalisés à l'Institut de Pédiatrie; ces enfants représentaient 95% des cas de poliomyélite paralytique aiguë recensés dans la ville.

Le diagnostic était posé d'après l'observation clinique (paralysie flasque asymétrique aiguë touchant les neurones moteurs inférieurs, sans troubles sensitifs, survenant à la suite d'un bref épisode de fièvre, et confirmée par coproculture, positive dans 60% des cas). Des témoins appariés selon l'âge et le sexe, et habitant également Madras, ont été recrutés parmi les consultants du secteur ambulatoire de l'Institut de Pédiatrie. Les cas et les témoins étaient considérés comme vaccinés s'ils avaient reçu les trois doses de TOPV avant l'âge de 6 mois. L'état vaccinal a été vérifié après le recrutement, si possible d'après des dossiers de vaccination. Une analyse cas-témoins sans appariement a été effectuée. Elle portait sur 78 cas et 315 témoins. L'efficacité du vaccin était de 81% (intervalle de confiance (IC) à 95%: 58–91%) chez les 6–35 mois et de 86% (IC 95%: 68–94%) chez les 6–23 mois. Après correction de l'âge selon la méthode de Mantel-Haenszel, elle était de 83% (IC 95%: 67–91%). Chez un enfant non vacciné, le risque de contracter une poliomyélite paralytique aiguë était cinq fois plus grand que chez un enfant ayant reçu les trois doses de vaccin.

References

1. **Santhanakrishnan, B.R. et al.** Poliomyelitis in children. *Indian journal of pediatrics*, **54**: 755–758 (1987).
2. **Sen, S. et al.** Poliomyelitis in vaccinated children. *Indian pediatrics*, **26**: 423–429 (1989).
3. **Lasch, E.E. et al.** Successful results of a program combining live and inactivated poliovirus vaccines to control poliomyelitis in Gaza. *Reviews of infectious diseases*, **6**: S467–470 (1984).
4. **Deivanayagam, N. & Nedunchelian, K.** Acute poliomyelitis in children: comparison of epidemiological and clinical features among immunized, partially immunized and unimmunized. *Indian pediatrics*, **28**: 609–613 (1991).
5. **John, T.J.** Antibody response of infants in tropics to 5 doses of oral polio vaccine. *British medical journal*, **3**: 811–812 (1976).
6. **Sokhey, J. et al.** Case definition in the surveillance of vaccine preventable diseases. *Indian pediatrics*, **25**: 599–609 (1988).
7. **Orenstein, W.A. et al.** Assessing vaccine efficacy in the field. *Epidemiological reviews*, **10**: 212–241 (1988).
8. **Balraj, V. et al.** Efficacy of oral polio vaccine in rural communities of North Arcot district, India. *International journal of epidemiology*, **19**: 711–714 (1990).
9. **Deming, M.S. et al.** Epidemic poliomyelitis in the Gambia following the control of poliomyelitis as an endemic disease. II. Clinical efficacy of trivalent oral polio vaccine. *American journal of epidemiology*, **135**: 393–408 (1992).
10. **Kim-Farley, R.J. et al.** Poliomyelitis surveillance and vaccine efficacy in Bombay, 1982–87. *Bulletin of the World Health Organization*, **67**: 663–667 (1989).
11. **Sutter, R.W. et al.** Outbreak of paralytic poliomyelitis in Oman: evidence for widespread transmission among fully vaccinated children. *Lancet*, **338**: 715–720 (1991).
12. **Kim-Farley, R.J. et al.** Outbreak of paralytic poliomyelitis, Taiwan. *Lancet*, **2**: 1322–1324 (1984).
13. **Singh, J. et al.** Epidemiological evaluation of oral polio vaccine efficacy in Delhi. *Indian journal of pediatrics*, **59**: 321–323 (1992).